

In the Claims

1. (Currently Amended) A method for producing DNA, wherein a the methylation analysis is used, comprising the steps of: characterized by that]

a) performing a genome-wide amplification is performed, and

b) using the amplificates generated in step a) are used as a standard in the methylation analysis.

2.(Original) The use of DNA produced by genome-wide amplification methods as a standard in the methylation analysis.

3.(Currently Amended) A method or the use according to of claim 1 or 2, characterized by that wherein the amplification methods performed are PEP, DOP-PCR or linker PCR are performed as an as amplification methods.

4. (Currently Amended) A method or the use according to of claim 1 or 2, characterized by that a wherein the amplification method performed is a multiple displacement amplification (MDA) is performed as an amplification method.

5.(Currently Amended) A method or the use according to of claim 4, characterized by that further comprising using a φ29 polymerase is used in the MDA.

6.(Currently Amended) A method or the use according to of claim 4, characterized by that the MDA is performed by means of further comprising using a commercially available kit.

7.(Currently Amended) A method or the use according to of claim 6, characterized by that wherein the commercially available kits are "GenomiPhi" (Amersham Biosciences) or "Repli-g" (Molecular Staging) is used as a kit.

8.(Currently Amended) A method or the use according to of claim 4, characterized by that further comprising a commercially available DNA produced by MDA is used as a standard.

9.(Currently Amended) A method or the use according to at least one of claims 1 – 8, characterized by that the methylation analysis is performed by of claim 1 further comprising using restriction enzymes.

10. (Currently Amended) A method or the use according to at least one of claims 1 – 8, characterized by that of claim 1 further comprising the methylation analysis is performed performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by methylation-specific ligation methods, MSP, Heavy Methyl or MethyLight.

11. (Currently Amended) A method or the use according to at least one of claims 1 – 8, characterized by that the methylation analysis is performed of claim 1 further comprising performing the methylation analysis after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by primer extension.

12. (Currently Amended) A method or the use according to at least one of claims 1 – 11, characterized by that the methylation

~~analysis is performed of claim 1 further comprising performing the methylation analysis~~ after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by an amplification and a hybridization of the amplificates at oligomer microarrays.

13. (Currently Amended) A method or the use according to at least one of claims 1 – 12, characterized by that ~~the methylation analysis is performed of claim 1 further comprising performing the methylation analysis~~ after conversion of the DNA into a form, in which methylated cytosines can be distinguished from non-methylated cytosines by means of hybridization, by means of a multiplex PCR.

14. (Currently Amended) A method or the use according to at least one of claims 1 – 13, characterized by that of claim 1 wherein a mixture of methylated and non-methylated DNA is used as a standard.

15. (Currently Amended) A method or the use according to at least one of claims 1 – 14, characterized by that of claim 1 wherein several mixtures of methylated and non-methylated DNA with different shares of methylated and non-methylated DNA are used as a standard.

16. (Currently Amended) A method or the use according to at least one of claims 1 – 15, characterized by that of claim 1 wherein the methylation analysis is performed for the diagnosis of cancer diseases or other diseases associated with a modification of the methylation status.

17. (Currently Amended) A method or the use according to at least one of claims 1 - 16, characterized by that of claim 1 wherein the methylation analysis is performed for the prognosis of desired or undesired effects of drugs and for the differentiation of cell types or tissues, or for the investigation of the cell differentiation.

18. (Currently Amended) A method for the determination of methylation rates of DNA samples by means of microarrays containing CG and TG oligomers, characterized by that comprising the steps of:

a) the arrays are hybridized hybridizing the arrays with two calibration standards, which have defined methylation rates;

b) using the hybridization values of step a) to determine a calibration curve for use as a suitable method of calculation; [by using the obtained hybridization values, a calibration curve is determined by means of a suitable method of calculation, and

c) the determining the actual methylation rates of the investigated DNA samples are determined by using this prepared calibration curve.

19. (Currently Amended) A method according to claim 18, characterized by that wherein the two calibration standards have methylation rates of 0% and 100%, respectively.

20. (Currently Amended) A method according to claim 18, characterized by that wherein more than two calibration standards are used, which have different methylation rates.

21. (Currently Amended) A method according to claim 18, characterized by that wherein the actual methylation rates are determined in a multi-stage calculation process, characterized by that comprising the steps of:

a) ~~a normalization of normalizing~~ the hybridization values is performed, whereby wherein methylation signals are determined,

b) ~~a normalization of normalizing~~ the methylation signals is performed with the aim of variance stabilization, and

c) ~~the determining the~~ methylation rates ~~are determined~~ by using the calibration standards and a suitable maximum likelihood algorithm.

22. (Currently Amended) A method according to claim 21, characterized by that before the normalization, further comprising a step prior to step a) wherein the hybridization values are corrected for the background noise inherent in the measurement method.

23. (Original) A kit comprising reagents for performing a WGA method or DNA amplified already by a WGA method and reagents for performing a bisulphite conversion, and optionally also containing a polymerase, primers and/or probes for an amplification and detection.

24. (Original) A methylated DNA produced by a WGA method and then methylated by means of an enzyme.

25. (Original) A methylated DNA produced by a WGA method and then methylated by means of the SssI methylase.

26. (Original) A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method.

27. (Original) A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 5 and 95%.

28. (Original) A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 10 and 80%.

29. (Original) A mixture of methylated and non-methylated DNA produced by a genome-wide amplification method, wherein the share of methylated DNA is between 25 and 75%.

30. (Currently Amended) The use of the DNA according to ~~claim 24 for the methylation analysis claims 24 to 25 or of a mixture according to claims 26 to 29 for the methylation analysis.~~

31. (Currently Amended) A method ~~or the use according to one of claims 1 to 17 claim 1~~, wherein the genome-wide amplification is performed by exclusively using nucleotides or nucleotide triphosphates, respectively, which are non-methylated.

32. (Original) A kit comprising reagents for performing a WGA method by exclusively using non-methylated nucleotides or non-methylated nucleotide triphosphates, respectively, or genomic DNA amplified by exclusively using non-methylated nucleotides or non-methylated nucleotide triphosphates, respectively, by WGA method, reagents for performing a bisulphite conversion,

and optionally at least one polymerase and primers for an amplification and/or probes for a detection.

33. (Original) An isolated methylated DNA or mixture of isolated methylated DNA fragments, respectively, obtainable by that genomic DNA is amplified by means of a WGA method by exclusively using non-methylated nucleotides or nucleotide triphosphates, respectively, and the amplified DNA or the mixture of amplified DNA fragments, respectively, is then methylated by means of an enzyme or the SssI methylase.

34. (Original) A mixture containing methylated and non-methylated DNA, preferably each from the same organism or from organisms of the same species, wherein the non-methylated DNA was obtained by means of a WGA method by using non-methylated nucleotides or nucleotide triphosphates, respectively, wherein optionally the share of methylated DNA is in the range between 5 and 95 mole-%, in particular between 10 and 80 mole-%, preferably between 25 and 75 mole-%, related to the total content of DNA.

35. (New) The use of the DNA according to claim to 25 for the methylation analysis.

36. (New) The use of the mixture according to claim 26 for the methylation analysis.

37. (New) The use of the mixture according to claim 27 for the methylation analysis.

38. (New) The use of the mixture according to claim 28 for the methylation analysis.

39. (New) The use of the mixture according to claim 29 for the methylation analysis.